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FORM PTO-1390 (REV 10-95) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

# TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY DOCKET NUMBER: 15675P364

U.S. APPLICATION NO. (If known, see 37 GER 1.5): 09/869692

| INTERNATIONAL APPLICATION NO. | INTERNATIONAL FILING DATE | PRIORITY DATE CLAIMED |
|---|---|---|
| PCT/FR99/03310 | December 29, 1999 | December 30, 1998 |

TITLE OF INVENTION
COSMETIC OR DERMATOLOGICAL COMPOSITION CONTAINING AN ACTIVE AGENT WHICH STIMULATES SYNTHESIS OF THE PROTEIN HSP 32 IN THE SKIN, AND COSMETIC TREATMENT METHOD

APPLICANT(S) FOR DO/EO/US
Carine Nizard; Marielle Moreau; Frederic Bonte

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371
3. ☐ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b)) and PCT articles 22 and 39(1).
4. ☐ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).
   a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☐ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

**Items 11. to 16. below concern document(s) or information included:**

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☐ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A subsequent specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☒ Other items or information:

priority request; copy of preliminary examination w/amended pages; English translation of new pages; English translation of preliminary examination report; forms PCT/IB301 & 304; PCT filing receipt; complete copy of application w/amended pages (17 pages)

| US APPLICATION NO. (if known) | INTERNATIONAL APPLICATION NO | ATTORNEY'S DOCKET NUMBER |
|---|---|---|
| 09/869692 | PCT/FR99/03310 | 15675P364 |

17. ☐ The following fees are submitted:

| | CALCULATIONS | FOR PTO USE ONLY |
|---|---|---|
| **BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5) ):** | | |
| Neither international preliminary examination fee (37 CFR 1.482 nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by EPO or JPO ..... **$1000.00** | | |
| International preliminary examination fee (37CFR1.482)not paid to USPTO but International Search Report prepared by the EPO or JPO.... **$860.00** | | |
| International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee paid to USPTO (37 CFR 1.445(a)(2)) ..... **$700.00** | | |
| International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) .... **$690.00** | | |
| International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) ..... **$100.00** | | |
| **ENTER APPROPRIATE BASIC FEE AMOUNT =** | $ 860.00 | |
| Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(e)). | $ | |

| CLAIMS | NUMBER FILED | | NUMBER EXTRA | RATE | | |
|---|---|---|---|---|---|---|
| Total claims | 28 | - 20 = | 8 | X **$18.00** | $ | 144.00 |
| Independent claims | 2 | - 3 = | 0 | X **$78.00** | $ | 0.00 |
| MULTIPLE DEPENDENT CLAIM(S) (if applicable) | | | | + **$270.00** | $ | 270.00 |
| **TOTAL OF ABOVE CALCULATIONS =** | | | | | $ | 1274.00 |
| Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also by filed (Note 37 CFR 1.9, 1.27, 1.28). | | | | | $ | |
| **SUBTOTAL =** | | | | | $ | 1274.00 |
| Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)). + | | | | | $ | |
| **TOTAL NATIONAL FEE =** | | | | | $ | 1274.00 |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property + | | | | | $ | |
| **TOTAL FEES ENCLOSED =** | | | | | $ | 1274.00 |
| | | | | | $ Amount to be: refunded | $ |
| | | | | | charged | $ |

a. ☒ A check in the amount of $ 1274.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. _____ in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 022666 . A duplicate copy of this sheet is enclosed.

**NOTE: Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.**

SEND ALL CORRESPONDENCE TO:

Blakely, Sokoloff, Taylor & Zafman LLP
12400 Wilshire Blvd. 7th Floor
Los Angeles, CA 90025-1026

SIGNATURE

6/29/01
NAME

38,139
REGISTRATION NUMBER

# COSMETIC OR DERMATOLOGICAL COMPOSITION CONTAINING AN ACTIVE AGENT WHICH STIMULATES SYNTHESIS OF THE PROTEIN HSP 32 IN THE SKIN, AND COSMETIC TREATMENT METHOD

The present invention relates to compositions, in particular dermato-cosmetological compositions, which are useful in the field of photoprotection, and to cosmetic methods for treating skin exposed to solar radiation.

Solar radiation, and mainly ultraviolet radiation, can cause harmful phenomena in the medium or long term. The solar energy reaching the ground is distributed, at wavelengths ($\lambda$) from 290 to 2 500 nm, for 50% in the infrared region ($\lambda$ = 800 to 2 500 nm), 40% in the visible region ($\lambda$ = 400 to 800 nm) and for 10% in the ultraviolet region, in which a distinction is made between the UVA region ($\lambda$ = 320-400 nm) and the UVB region ($\lambda$ = 290-320 nm).

Although immediate (UVA) or delayed (UVB) pigmentation constitutes a natural means of defense of the skin, exposure to ultraviolet radiation may cause actinic erythema, epidermal hyperplasia, cutaneous senescence (or solar elastosis) and even, in certain cases, may promote the onset of skin cancers.

Although the majority of the UVB radiation is absorbed by the horny layer, 10% reaches the dermis; the majority of the UVA radiation (and some of the visible radiation) crosses the epidermis and 20 to 30% reaches the dermis, where it may cause adverse changes in the skin cells.

It is accepted that UVA radiation causes the production of reactive oxygen species, in particular via the intracellular generation of $H_2O_2$ (Morlière et al., 1992).

The compounds have many target cells and cause various types of damage:

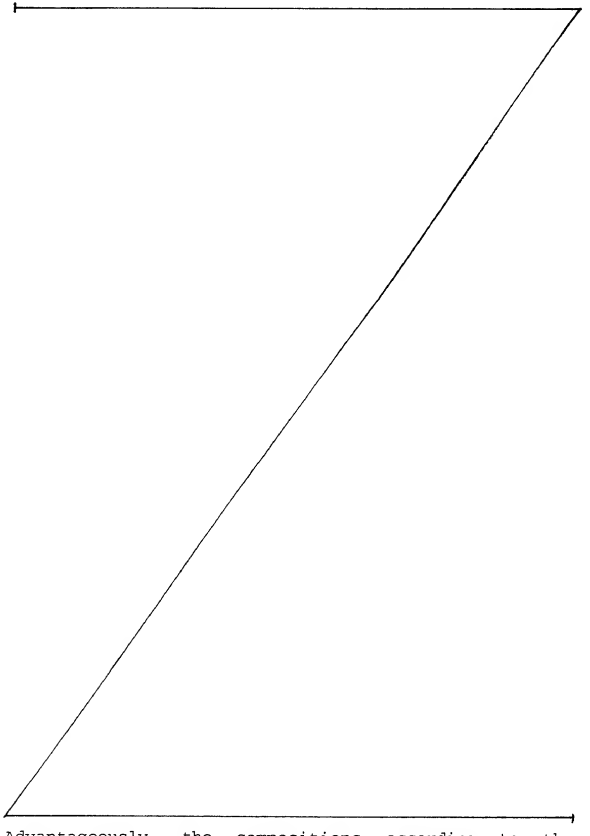
- DNA: single- or double-strand cleavages, DNA-protein bridging,
- proteins: singlet oxygen reacts with certain residues, including histidine and tryptophan,
- membranes: peroxidation of polyethylenic fatty acids.

These adverse changes take place on all types of skin cells, in particular keratinocytes, melanocytes and fibroblasts, and are generally inflammatory manifestations or manifestations of actinic ageing (wrinkles).

It is also acknowledged that "HSPs" ("heat shock proteins") have been demonstrated on cells, both eukaryotic and prokaryotic cells, subjected to physiological stress, in particular heat stress, both in vivo and in vitro. These cells react by expressing a set of proteins which vary in number and size depending on the target organism and the inducing stress (Maytin, 1995; Milarski et al., 1989).

HSPs are classed in families according to their molecular weight. HSP 90, HSP 70, HSP 60 and HSP 30 have thus been distinguished. Many of the genes encoding the HSPs have been sequenced and their chromosomal location determined; however, little information is currently available regarding the transcriptional control of these molecules which are suspected of being among the cellular devices for protecting against a toxic environment.

Many factors may cause the induction of HSPs: high temperatures, heavy metals, viral infections, alcohol, growth factors and low temperatures (Simon et al.,





Advantageously, the compositions according to the invention contain at least one UVA-ray and/or UVB-ray screening agent. These screening agents are well known to those skilled in the art. Mention may be made, for

example, of benzophenones, such as 2,2',4,4'-tetrahydroxybenzophenone or Benzophenone-2 and 2-hydroxy-4'-methoxybenzophenone or Eusolex 4360®, which absorbs UVA and UVB radiation, cinnamate derivatives such as octyl p-methoxycinnamate or Parsol MCX®, which absorbs UVB radiation, dibenzoylmethane derivatives such as 4-tert-butyl-4'-methoxydibenzoylmethane or Parsol 1789®, which absorbs UVA radiation, and para-aminobenzoic acid (Paba) esters, such as octyldimethyl PABA or Escalol 507®, which absorbs UVB radiation.

In this regard, it is important to note that the fibroblasts, which are major cells of the dermis giving the skin its tonicity, are the only skin cells in which it is particularly advantageous to induce the production of the protein HSP 32. It is thus particularly advantageous, in order to restore or conserve a good physiological condition of the skin, to stimulate the formation of this protein by the fibroblasts.

Consequently, the present invention also relates to the use of a compound capable of activating the endogenous synthesis of HSP 32, for the preparation of a cosmetic composition for protecting fibroblasts. Among the compounds described in the prior art which are capable of activating the synthesis of HSPs in general, mention should be made of patent application FR 2 757 863 which describes the use of biological substances of plant origin extracted from the fruit of plants with CAM metabolism.

Among the compounds capable of promoting the endogenous production of HSP 32 by the fibroblasts, mention may be made of caffeic acid esters and derivatives thereof, in particular oraposide which has been described in documents WO 92/16544, FR 2 652 086, FR 2 708 851 and FR 2 699 818, and also PCOs (procyanidol oligomers)

which have been described in documents EP 953 353, EP 955 051 and EP 397 914 and the article by J. Masquelier (1990, Parfums, cosmétiques, arômes No. 95, pp. 89-97) and which may be extracted from grape and from green tea, for example, and also derivatives thereof.

Among the PCO derivatives which may be used, mention should also be made of the crosslinked PCOs as described in patent US 5 780 060.

The compounds according to the present invention will preferably be used at concentrations of between 0.1% and 5% by weight of the composition and preferably at concentrations of between 0.2% and 1% by weight.

The compositions according to the present invention may comprise combinations of several "activating" compounds, as well as combinations with other advantageous components.

Among the preferred combinations, mention should be made more particularly of those which contain at least one compound chosen from:

- forskolin or any extract containing it, in particular extracts of Plecthantrus barbatus,
- tyrosine and its derivatives, in particular malyltyrosine,
- ellagic acid and its derivatives or any extract containing them,
- extracts of Centella asiatica, of Potentilla erecta and of Eriobotrya japonica,
- soybean saponins and alfalfa saponins such as soyasapogenols,
- isoflavones, in particular formononetin, daidzein and genistein or mixture thereof,
- vitamin C and its derivatives, in particular vitamin C magnesium phosphate, tocopherol and its

esters, in particular tocopheryl gentisate and tocopheryl phosphate,
- 18-β-glycyrrhetinic acid,
- extracts of Azadiracta indica,
- curcuminoids, in particular a curcumin.

It is advantageous to note that the compositions according to the present invention can also contain heat shock proteins, in particular the protein HSP 32 itself or an active fragment thereof.

Preferably, the compositions according to the present invention will be in a form which is suitable for topical cutaneous administration.

These compositions may especially be in the form of solutions, suspensions, lotions, milks, gels, creams, O/W or W/O emulsions or multiple emulsions, sticks or powders, suitable for application to the skin, the lips and/or the hair.

They comprise the excipients required for this formulation, such as solvents, diluents, thickeners, ionic or nonionic surfactants, in particular sucroesters, preserving agents, antioxidants, colorants, fragrances or, when they are packaged as aerosols, propellant gases.

The compositions may also contain softeners, moisturizers, anti-inflammatory agents, anti-wrinkle agents, in particular agents promoting the synthesis of glycosamino-glycan (GAG), or tanning activators.

Advantageously, the compositions according to the invention contain a free-radical scavenger, for example α-tocopherol or its esters.

According to one of the embodiments of the invention, the composition also contains at least one photoprotective agent, preferably chosen from the group consisting of physical sunblocks and sunscreens.

Sunscreens are molecules capable of absorbing radiation within a more or less broad region of the solar spectrum. They may belong to various classes; mention may be made, in a non-limiting manner, of para-aminobenzoic acid and its derivatives, cinnamic acid esters, salicylic acid derivatives or benzylidenecamphor derivatives, benzimidazoles and benzophenone derivatives.

The physical sunblocks which may be used are, in particular, titanium oxide, zinc oxide, mica derivatives and talc.

The presence of physical sunblocks or sunscreens in the composition will make it possible to improve the protection against solar radiation of the body surface onto which it is applied.

A subject of the invention is also the use of at least one compound chosen from the group consisting of PCOs and derivatives thereof, caffeic acid esters and derivatives thereof and mixtures of these compounds, for the preparation of a composition intended to activate the endogenous synthesis of HSP 32 or a functional peptide fragment of such a protein.

The preferential aspects stated above for the composition per se are also valid for the composition prepared and intended to activate the endogenous synthesis of HSP 32 or a functional peptide fragment of such a protein according to this use. In particular, the use according to the invention is characerized in

that the composition contains pharmaceutically and/or cosmetologically acceptable excipients.

Another subject of the invention is a cosmetic method for treating the skin and integuments in order to protect them against the harmful effects of radiation, in particular ultraviolet radiation, characterized in that an effective amount of a composition as described above is applied locally, before or at the time of exposure to radiation, in particular ultraviolet radiation, for example solar radiation.

More particularly, the above method is intended to combat the formation of solar erythema, solar allergies or solar elastosis and to prevent or delay the appearance of wrinkles caused by the harmful effects of ultraviolet radiation.

Finally, according to another of its aspects, the invention comprises the use of these compositions as medicinal products, in particular in dermatology.

A subject of the invention is also the application, as a cosmetic product, of the heat shock protein HSP 32.

In the examples which follow, the protective effect of PCOs by means of inducing HSP 32 will be demonstrated as a function of an administration or otherwise of UVA.

**EXAMPLE 1**

The following examples were carried out using fibroblast cell cultures which are or are not subjected to the treatment with PCOs and then on which, after UVA radiation, the induction of HSP 32 is assayed by means known to those skilled in the art.

These means in particular comprise the use of an anti-HSP 32 primary antibody, commercially available from

the company TEBU, in a technique known as immunodetection.

The results obtained are collated in the table below.

Effect of PCO on the expression of the protein HSP 32 with or without UVA (Western blot)

| | CONTROL | | PCO 25 µg/ml | | PCO 50 µg/ml | |
|---|---|---|---|---|---|---|
| | UV - | UV + | UV - | UV + | UV - | UV + |
| Volume density | 95 832 | 125 208 | 140 935 | 123 165 | 163 328 | 195 552 |
| Effect/control UV- | 100% | 131% | 147% | 128% | 170% | 204% |

It is found that the UVA naturally induces the synthesis of HSP 32 (protein quantified by Western blot) but this synthesis remains moderate. The addition of PCO stimulates the induction of the HSP 32 molecules more strongly than UVA alone, in particular when the PCOs are used at 50 µg/ml.

Treating the cells with PCOs followed by UVA irradiation leads to a massive stimulation of the production of HSP since it may be up to 204% when the PCOs are used at 50 µg/ml.

The protective effect of these PCOs is thus clearly demonstrated, both with and without irradiation. Thus, the compositions may be used preventively and/or curatively, preferably in combination with UVA-stabilizing and/or UVB-stabilizing screening agents.

| | |
|---|---|
| - Extract of Centella asiatica | 0.5 |
| - Octyl methoxycinnamate | 2 |
| - Excipient, qs | 100 |

**BIBLIOGRAPHY**

Maytin, E.D. (1995). J. Invest. Dermato. **104**, 448-454.

Milarski, K.L., Welch, W.J., and Morimoto, R.I. (1989), J. Cell. Biol. **108**, 413-424.

Morliere, P., Moysan, A., Gaboriau, F., Santus, R., Mazière, J.C., and Dubertret, L. (1992). Path. Biol. **40**, 160-168.

Simon, M.M., Reikerstorfer, A., Schwarz, A., Krone, C., Luger, T., Jäättelä, A., and Scharz, T. (1995). J. Clin. Invest. **95**, 926-933.

**CLAIMS**

1. Use of at least one compound chosen from the group consisting of PCOs and derivatives thereof, caffeic acid esters and derivatives thereof and mixtures of these compounds, for the preparation of a composition intended to activate the endogenous synthesis of HSP 32 or a functional peptide fragment of such a protein.

2. Use according to Claim 1, characterized in that the composition contains at least one UVA-stabilizing and/or UVB-stabilizing screening agent.

3. Use according to Claim 1 or 2, characterized in that the PCO derivative is a crosslinked PCO.

4. Use according to any one of the preceding claims, characterized in that the PCO is a PCO from grape seed or a PCO from green tea.

5. Use according to Claim 1 or 2, characterized in that the caffeic acid ester is oraposide.

6. Use according to any one of the preceding claims, characterized in that the composition contains pharmaceutically and/or cosmetologically acceptable excipients.

7. Use according to Claim 6, characterized in that the excipients are suitable for external topical administration.

8. Use according to one of Claims 1 to 7, characterized in that said compound is present in a concentration of between 0.1% and 5% w/w in the composition.

9. Use according to Claim 8, characterized in that said compound is present in a concentration of between 0.2% and 1% w/w in the composition.

10. Use according to one of Claims 1 to 9, characterized in that the composition also contains at least one other photoprotective agent.

11. Use according to one of Claims 7 to 10, characterized in that the composition contains at least one compound chosen from the group consisting of physical sunblocks, sunscreens and free-radical scavengers.

12. Use according to one of Claims 1 to 11, characterized in that the composition also contains at least one component chosen from:

- forskolin or any extract containing it, in particular extracts of Plecthantrus barbatus,
- tyrosine and its derivatives, in particular malyltyrosine,
- ellagic acid and its derivatives or any extract containing them,
- extracts of Centella asiatica, of Potentilla erecta and of Eriobotrya japonica,
- soybean saponins and alfalfa saponins such as soyasapogenols,
- isoflavones, in particular formononetin, daidzein and genistein or mixture thereof,
- vitamin C and its derivatives, in particular vitamin C magnesium phosphate, tocopherol and its esters, in particular tocopheryl gentisate and tocopheryl phosphate,
- 18-β-glycyrrhetinic acid,
- extracts of Azadiracta indica,
- curcuminoids, in particular a curcumin.

13. Use according to one of Claims 1 to 12, characterized in that the composition also contains the protein HSP 32 or an active fragment thereof.

14. Use of at least one compound according to Claims 1 and 3 to 5, which is capable of activating the endogenous synthesis of HSP 32 or a functional peptide fragment of such a protein, in combination with at least one component chosen from:

- forskolin or any extract containing it, in particular extracts of Plecthantrus barbatus,
- tyrosine and its derivatives, in particular malyltyrosine, with the exception of L-DOPA (or "3-hydroxy-L-tyrosine"),
- ellagic acid and its derivatives or any extract containing them,
- extracts of Centella asiatica, of Potentilla erecta and of Eriobotrya japonica,
- soybean saponins and alfalfa saponins such as soyasapogenols,
- isoflavones, in particular formononetin, daidzein and genistein or mixture thereof,
- vitamin C and its derivatives, in particular vitamin C magnesium phosphate, tocopherol and its esters, in particular tocopheryl gentisate and tocopheryl phosphate,
- 18-β-glycyrrhetinic acid,
- extracts of Azadiracta indica,
- curcuminoids, in particular a curcumin,

with pharmaceutically and/or cosmetically acceptable excipients, for the preparation of a composition intended for dermatological or cosmetological use.

15. Use according to Claim 14, characterized in that it contains at least one UVA-stabilizing and/or UVB-stabilizing screening agent.

16. Use according to either of Claims 14 and 15, characterized in that the excipients are suitable for external topical administration.

17. Use according to one of Claims 14 to 16, characterized in that said compound is present in a concentration of between 0.1% and 5% w/w in the composition.

18. Use according to Claim 17, characterized in that said compound is present in a concentration of between 0.2% and 1% w/w in the composition.

19. Use according to one of Claims 14 to 18, characterized in that it also contains at least one other photoprotective agent.

20. Use according to one of Claims 16 to 19, characterized in that it contains at least one compound chosen from the group consisting of physical sunblocks, sunscreens and free-radical scavengers.

21. Use to one of Claims 14 to 20, characterized in that it also contains the protein HSP 32 or an active fragment thereof.

22. Cosmetic method for treating the skin or integuments in order to protect them against the harmful effects of radiation, in particular ultraviolet radiation, characterized in that an effective amount of at least one cosmetic composition according to one of Claims 14 to 21 is applied locally, before or at the time of exposure to said radiation.

23. Method according to Claim 22, characterized in that it is intended to combat the formation of solar erythema, solar allergies or solar elastosis.

24. Method according to Claim 22, characterized in that it is intended to prevent or delay actinic ageing of the skin, in particular to prevent or delay the appearance of wrinkles caused by the harmful effects of ultraviolet radiation.

25. Application, as a cosmetic product, of the heat shock protein HSP 32.

26. Use of a compound capable of activating the endogenous synthesis of HSP 32, as defined in one of Claims 1 and 3 to 5, for the preparation of a cosmetic composition for protecting fibroblasts.

Our ref.: 15675. P364

# DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below, next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

Cosmetic or dermatological composition containing an active agent with stimulates synthesis of the protein HSP 32 in the skin, and cosmetic treatment method

the specification of which

is attached hereto
was filed on December 29, 1999
Application Serial No. PCT FR99/03310
And was amended on
(if applicable)

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above. I do not know and do not believe that the same was ever known or used in the United States of America before my invention thereof, or patented or described in any printed publication in any country before my invention thereof or more than one year prior to this application, that the same was not in public use or on sale in the United States of America more than one year prior to this application, and that the invention has not been patented or made the subject of an inventor's certificate issued before the date of this application in any country foreign to the United States of America on an application filed by me or my legal representatives or assigns more than twelve months prior to this application.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, Section 1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, Section 199, of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor(s) certificate having a filing date before that of the application on which priority is claimed:

| Prior Foreign Application(s) | | | Priority Claimed | |
|---|---|---|---|---|
| 98/16641 (Number) | FRANCE (Country) | 30.12.1998 (Day/Month/Year Filed) | X Yes | No |
| (Number) | (Country) | (Day/Month/Year Filed) | Yes | No |
| (Number) | (Country) | (Day/Month/Year Filed) | Yes | No |

I hereby claim the benefit under Title 35, United States Code, Section 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, Section 112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, Section 1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application.

PCT/FR99/03310 (Application Serial No.) December 29, 1999 (Filing Date) (pending )

(Application Serial No.) (Filing Date) (Status - patented, pending, abandoned)

(Application Serial No.) (Filing Date) (Status - patented, pending, abandoned)



I hereby appoint BLAKELY, SOKOLOFF, TAYLOR & ZAFMAN, a firm including :
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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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